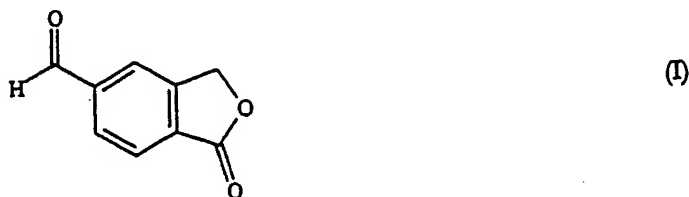


II. Claims

1) (Currently Amended) A process for the preparation of citalopram which comprises:

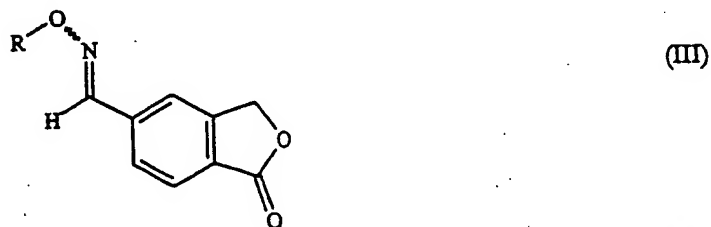
(a) treating 5-formylphthalide of formula



with a hydroxylamine of formula

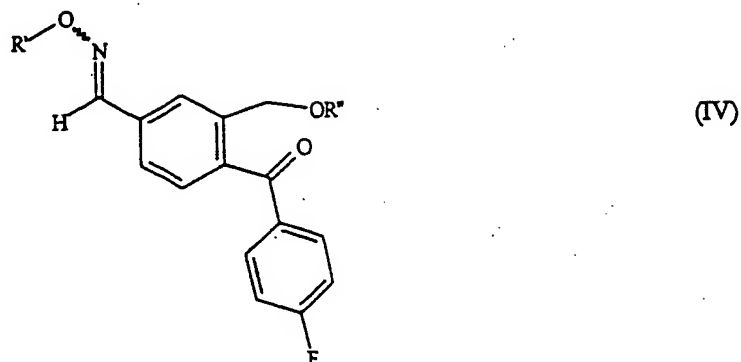


wherein R represents a hydrogen atom (IIa) or a substituent R' inert under the conditions of a Grignard reaction (IIb) and where R' is not hydrogen, to obtain an oxime of formula



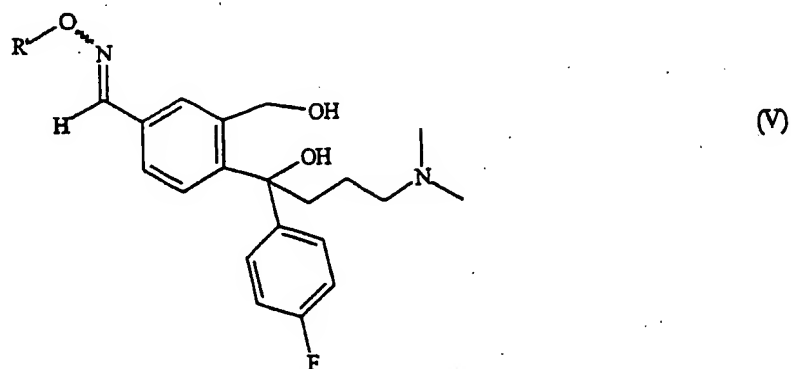
wherein R is as defined above, with a 4-fluorophenylmagnesium halide, when R=R' (IIIb) or after substitution of R by R' when R=H (IIIa);

(b) reacting the oxime thus obtained to form an intermediate ketone of formula



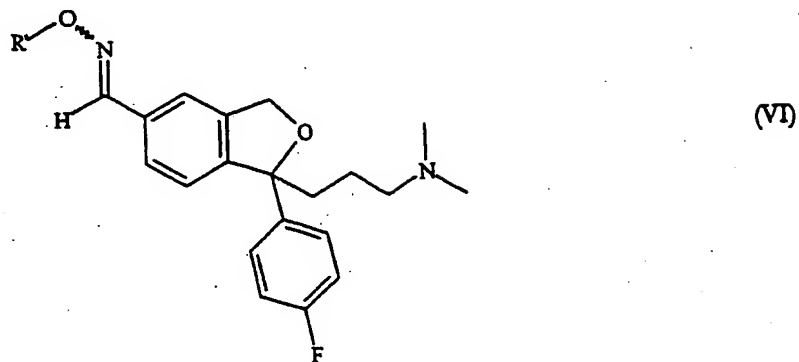
wherein R' is as defined above and R'' represents MgHal (IVa) wherein Hal is halogen, or hydrogen (IVb), with a [3-(dimethylamino)propyl]magnesium halide;

(c) reacting the intermediate ketone of formula IV to form an intermediate diol of formula



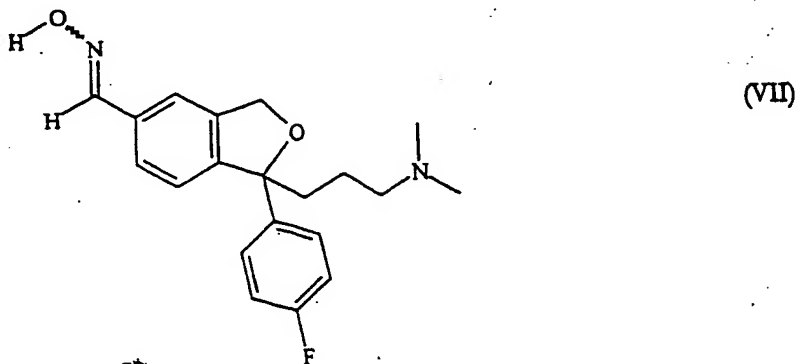
wherein R' is as defined above; and

(d) cyclizing the intermediate diol of formula V to form a substituted oxime of formula



wherein R' is as defined above;

(e) removing the group R' of the substituted oxime of formula VI to form the unsubstituted oxyamino group of the oxime of formula



(f) converting the unsubstituted oxyamino group of the oxime of formula VII into nitrile to give citalopram (A) or one of its pharmaceutical acceptable salts; or

(e') optionally, when R' is triphenylmethyl or diphenylmethyl, converting the substituted oxyamino group of the oxime of formula VI into nitrile by treatment with a mixed anhydride of formula



wherein R''' represents a C₁-C₆ alkyl group, an aralkyl group or an aryl group, to give citalopram (A) or a pharmaceutical acceptable salt thereof.

- 2) **(Original)** The process according to claim 1, wherein R' is (C₁-C₆)alkyl, (C₁-C₃)alkoxy(C₂-C₄)alkyl, a benzyl, diphenylmethyl or triphenylmethyl group, unsubstituted or substituted on the benzene rings with one or more groups independently chosen among (C₁-C₆) alkyl, (C₁-C₃)alkoxy and nitro groups or with a 2,3- or 3,4-methylenedioxy group.
- 3) **(Original)** A process according to claim 2 wherein R' is triphenylmethyl or diphenylmethyl.
- 4) **(Original)** A process according to claim 1 wherein said 4-fluorophenylmagnesium halide is the bromide.
- 5) **(Original)** A process according to claim 1 wherein said [3-(dimethylamino)propyl]magnesium halide is the chloride.
- 6) **(Original)** A process according to claim 1 wherein step (d) is carried out in the presence of a halide of an alkyl- or arylsulfonic acid.
- 7) **(Original)** A process according to claim 6 wherein said halide of an alkyl- or arylsulfonic acid is methanesulfonyl chloride.
- 8) **(Previously Presented)** A process according to claim 1 wherein R' represents triphenylmethyl or diphenylmethyl and the intermediate of formula VI is converted to citalopram according to step (e').
- 9) **(Original)** A process according to claim 8 wherein in said anhydride of formula VIII R''' represents (C₁-C₄) alkyl, benzyl or phenyl.

- 10) **(Original)** A process according to claim 9 wherein R''' represents methyl.
- 11) **(Original)** A process according to claim 10 wherein said anhydride of formula VIII is used in admixture with acetic acid.
- 12) **(Original)** A process according to claim 11 wherein said mixture is prepared from formic acid and acetic anhydride in a molar ratio of 1:1.25.
- 13) **(Original)** A process according to claim 1 wherein said compound of formula VIII is used in 1.25 moles per mole of compound of formula VI.
- 14) **(Original)** A process according to claim 1 wherein citalopram is isolated in the form of hydrobromide.
- 15) **(Withdrawn)** A compound of formula III, wherein R represents hydrogen or a substituent R' inert under the conditions of a Grignard reaction.
- 16) **(Withdrawn)** A compound according to claim 15 wherein R represents a substituent R' selected between triphenylmethyl and diphenylmethyl.
- 17) **(Withdrawn)** A compound of formula N wherein R' represents hydrogen or a substituent inert under the conditions of a Grignard reaction and R'' represents MgHal (IVa), wherein Hal is halogen, or hydrogen.
- 18) **(Withdrawn)** A compound according to claim 17 wherein R' is triphenylmethyl or diphenylmethyl.
- 19) **(Withdrawn)** A compound of formula V wherein R' represents hydrogen or a substituent inert under the conditions of a Grignard reaction.

20) (Withdrawn) A compound according to claim 19 wherein R' is triphenylmethyl or diphenylmethyl.

21) (Withdrawn) A compound of formula VI wherein R' represents a substituent inert under the conditions of a Grignard reaction, other than methyl.

22) (Withdrawn) A compound according to claim 21 wherein R' is triphenylmethyl or diphenylmethyl.

23) (Withdrawn) Use of the compounds of formula III, IV, V and VI as intermediates for the preparation of citalopram.

24) (Original) A process for preparing citalopram, according to claim 1, as a single enantiomer characterized in that the corresponding isolated enantiomers of the compounds of formula V or VI are used as intermediates.

25) (Currently Amended) A process according to claim 24, characterized in that the isolated enantiomers of compounds of formula V or VI are prepared by resolution of the corresponding racemic mixtures with an optically active acids; acid selected from the group consisting of tartaric acid and camphosulfonic acid.

26) (Withdrawn) A compound according to claims 19 to 22 as a single enantiomer.

27) (Previously Presented) A process according to claim 24, characterized in that the isolated enantiomers of compounds of formula V or VI are prepared by resolution of the corresponding racemic mixtures with an optically active acid selected from tartaric or camphosulfonic acids.

28) (Previously Presented) The process of claim 1 where R' in formula III, represents hydrogen or a substituent R' inert under the conditions of a Grignard reaction.

29) (Previously Presented) The process of claim 1 where R' in formula III is triphenylmethyl or diphenylmethyl.

30) (Previously Presented) The process of claim 1 where R' in formula IV represents hydrogen or a substituent inert under the conditions of a Grignard reaction and R'' represents MgHal (IVa), wherein Hal is halogen, or hydrogen.

31) (Previously Presented) The process of claim 1 where R' in formula V represents hydrogen or a substituent inert under the conditions of a Grignard reaction.

32) (Previously Presented) The process of claim 1 where R' in formula VI represents a substituent inert under the conditions of a Grignard reaction, other than methyl.

33) (Previously Presented) The process of claim 1 where R' in formula VI is triphenylmethyl or diphenylmethyl.